EFFICACY REVIEW

Product(s): **Kaput Rat and Mouse Bait**

Date: October 22, 2004

EPA File Symbol(s): 72500-6

DP Bar code(s): D305560

Chemical Code: 086002 Warfarin

Formulation(s): Grain Bait Placepacks (0.025% Warfarin)

Purpose for Review: The purpose for this review is to evaluate two efficacy studies sent in to support the use of placepacks for the currently registered product. The original product was registered September 8, 2003.

MRID No(s):

463089-01 Mach, J. June 11, 2004. Standard House Mouse (Mus musculus) Anticoagulant Placepack Dry Bait Laboratory Test Method with Kaput Rat and Mouse Bait (0.025% Warfarin). 1.218 (7-28-91). Genesis Laboratories, Inc. Unpublished Report. Study number 03031. 90pp.

463089-02 Mach, J. June 11, 2004. Standard Norway Rat (Rattus norvegicus) Anticoagulant Placepack Dry Bait Laboratory Test Method with Kaput Rat and Mouse Bait (0.025% Warfarin). 1.217 (9-3-92). Genesis Laboratories, Inc. Unpublished Report. Study number 03030. 90pp.

Good Laboratory Practices: Yes

Branch Chief: Meredith Laws

Team Leader: John Hebert, Product Manager 07

IRB Reviewer: Geraldine R. McCann, Biologist

BACKGROUND: A previous review was done for this product by G. McCann on May 30, 2003. The original MRIDs associated with this product were 456629-01, 456629-03, and 456629-04. Bait composition, bait storage in the freezer, and the OPP guidelines were not followed in the above mentioned MRIDs. The studies were found to be ungradable and more information was obtained to rectify the unacceptable studies. The information to complete the MRIDs listed was pin punched June 26, 2003, (MRID 460178-00).

REVIEW OF DATA:

1. **463089-01** Mach, J. June 11, 2004. Standard House Mouse (Mus musculus) Anticoagulant Placepack Dry Bait Laboratory Test Method with Kaput Rat and Mouse Bait (0.025% Warfarin). 1.218 (7-28-91). Genesis Laboratories, Inc. Unpublished Report. Study number 03031. 90pp.

The purpose of this study as described by Mach is to investigate the laboratory effectiveness of Kaput Rat and Mouse Bait in placepacks for laboratory house mice.

Mach describes the product (Kaput Rat and Mouse placepacks) as formulated grain bait added to placepacks. He reports that the "test substance was formulated ... by Scimetrics, Ltd. It was logged into an ambient temperature storage locker (TS-2) as 03-TS-38A, B, and C that had a temperature range of 14 to 22 °C (11/26/03 to 1/25/04). All three lots of bait were used for the study to maintain a consistent supply. The first lot of the bait was not enough to complete the study so a second lot, "B", was formulated The average placepack weighed 59 grams. The paper material used for the placepack weighed 1.89 grams. The average bait contained in the placepack was 57.11 grams. The three formulations used in this test (batch/lot numbers: 61126031, 60107041, and 60108041) correspond to the CSF dated May 31, 2002, for the product 72500-6. The test substance formula is presented in a Confidential Attachment (Cross reference #1)." **In a supplemental memo sent to the Agency, the information is provided in type rather than from the analytical notebook to link the analysis to the bait formulated with the analytical records and their chromatographic records.**

Mach indicates that the trial was run according to the OPP guideline 1.218: Standard House Mouse Anticoagulant Placepack Dry Bait Laboratory Test Method. Protocol 1.218 is appropriate for screening placepacks for efficacy against house mice. This protocol dictates exposure of test-group animals to a choice between EPA challenge diet and placepacks for a period of 15 days for an anticoagulant rodenticide, followed by 5 days of follow-up observation during which time EPA challenge diet is to be the only food offered. Mach ran a control group and two groups of mice exposed to packaged bait. (No claims of weather-resistance are proposed for 72500-6).

For this study, there were 10 group housed males and 10 group housed female Swiss Webstar-strain mice per test group times 2 test groups for a total of 40 test mice and 10 group housed males and 10 group housed female control mice. Sixty-eight mice arrived at the test facility on December 29, 2003, to begin the

pre-test holding period. They were placed 11 or 12 to a tank. The housing units were stock tanks measuring 4x2x2 feet (7.14 ft^2). Heat and humidity were monitored with a NIST traceable, digital thermo/hygro unit with a lead placed in a pint of propylene glycol. Minimum and Maximum readings were recorded. Temperatures ranged from a minimum temperature of 19 °C to 25 °C (average temperature 22 °C, 71.6 °F) and the humidity ranged between 19 and 79% with the average humidity between 40.42% and 73.04%.

The Rep I test-group males (10) weighed 16.5 g to 18.7 g (mean = 17.65 g) at the start of the test, while the Rep I females (10) weighed 18.0 g to 22.1 g (mean = 20.23 g). The Rep II test-group males (10) weighed 18.8 g to 24.1 g (mean = 21.61 g) at the start of the test, while the Rep I females (10) weighed 17.3 g to 23.4 g (mean = 18.67 g). The 0.18 g difference in mean weights between the sexes of the tested groups did not exceed the 5 g maximum that Protocol 1.218 permits for trials in which laboratory mice are used as subjects. The subjects were within the allowable weight range of 15 to 35 g. The control group was similarly comprised, with the males averaging 21.86 g (range 24.7-28.3 g) and the females 20.42 g (range 21.1-24.1 g) at the start of the study.

The bait-exposure phase of the bioassay began on 1/5/2004.

Results of the trial are summarized Tables 1 and 2. All test-group animals died within 8 days of the onset of exposure to toxic bait. The 90% mortality criterion for a trial with fresh bait was met. No mortalities were reported for the control group.

Mean body weights as reported by Mach were for the control mice, at the termination of the study, 26.3 g for the males and 22.4 g for the females. The mean body weights at death, of the male and female mice in each of the treatment groups were 20.6 g and 17.7 g (replicate I) and 21.6 g and 18.2 g (replicate II), respectfully.

Mach reports "The control group was offered the OPP rat and mouse challenge diet ad libitum for the entire exposure and post test period. Consumption of the challenge diet was not measured. The treatment group, replicate I mice consumed 10 placepacks (or about 571.1 g) of Kaput Rat and Mouse Bait during the exposure period. The treatment group, replicate II mice consumed 13 placepacks (or about 742.5 g) of Kaput Rat and Mouse Bait during the exposure period." page 13 of 90.

The test results are summarized below:

Table 1. Kaput Rat and Mouse Bait Placepacks (0.025% Warfarin) on Mice (Rep I)

	Pretest Weights	**15-Day Test-Consumption and Mortality**		
Sex	**Average Group Weight (g)**	**OPP Diet Consumed (g)**	**Treated Bait Consumed (g)**	**Total Bait Consumption (g)**

M (10)	17.23	NA	571.1	NA
F (10)	20.23	**100% Mortality**		Percent **Toxic Bait** Consumed NA
Total (20)	Group Difference 2.58			

Table 2. Kaput Rat and Mouse Bait Placepacks (0.025% Warfarin) on Mice (Rep II)

	Pretest Weights	**15-Day Test-Consumption and Mortality**		
Sex	**Average Group Weight (g)**	**OPP Diet Consumed (g)**	**Treated Bait Consumed (g)**	**Total Bait Consumption (g)**
M (10)	21.61	NA	742.4	NA
F (10)	18.67	**100% Mortality**		Percent **Toxic Bait** Consumed NA
Total (20)	Group Difference 2.94			

2. **463089-02** Mach, J. June 11, 2004. Standard Norway Rat (Rattus norvegicus) Anticoagulant Placepack Dry Bait Laboratory Test Method with Kaput Rat and Mouse Bait (0.025% Warfarin). 1.217 (9-3-92). Genesis Laboratories, Inc. Unpublished Report. Study number 03030. 90pp.

The purpose of this study as described by Mach is to investigate the laboratory effectiveness of Kaput Rat and Mouse Bait in placepacks for laboratory Norway rats.

Mach describes the product (Kaput Rat and Mouse placepacks) as formulated grain bait added to placepacks. He reports that the "test substance was formulated ... by Scimetrics, Ltd. It was logged into an ambient temperature storage locker (TS-2) as 03-TS-38A, B, and C that had a temperature range of 14 to 22 °C (11/26/03 to 1/25/04). All three lots of bait were used for the study to maintain a consistent supply. The first lot of the bait was not enough to complete the study so a second lot, "B", was formulated The average placepack weighed 59 grams. The paper material used for the placepack weighed 1.89 grams. The average bait contained in the placepack was 57.11 grams. The three formulations used in this test (batch/lot numbers: 61126031, 60107041, and 60108041) correspond to the CSF dated May 31, 2002, for the product 72500-6. The test substance formula is presented in a Confidential Attachment (Cross reference #1)." **In a**

supplemental memo sent to the Agency, the information is provided in type rather than from the analytical notebook to link the analysis to the bait formulated with the analytical records and their chromatographic records.

Mach indicates the trial was run according to the OPP guideline 1.217: Standard Norway Rat Anticoagulant Placepack Dry Bait Laboratory Test Method, appropriate for screening placepacks for efficacy against Norway rats. This protocol dictates exposure of test-group animals to a choice between EPA challenge diet and placepacks for a period of 15 days for an anticoagulant rodenticide, followed by 5 days of follow-up observation during which time EPA challenge diet is to be the only food offered. Mach ran a control group and two groups of rats exposed to packaged bait. (No claims of weather-resistance are proposed for 72500-6).
For this study, there were 10 group housed males and 10 group housed female Wistar strain per test group times 2 test groups for a total of 40 test rats and 10 group housed males and 10 group housed female control rats. Sixty rats arrived at the test facility on December 29, 2003, to begin the pre-test holding period. They were placed 30 same sex animals to a tank for pre-test holding and were randomly assigned to groups for test room acclimation. The housing units were arenas or tanks measuring 7.29 x 2.54 feet (18.52 ft^2). Heat and humidity were monitored with a NIST traceable, digital thermo/hygro unit with a lead placed in a pint of propylene glycol. Minimum and Maximum readings were recorded. Temperatures ranged from a 15 °C to 24 °C (average temperature 20 °C, 71.6 °F) and the humidity ranged between 44 and 65% with the average humidity between 40.42% and 73.04%. No raw data was presented in the

The rats were all weighed on January 2, 2004. Rep I test-group males (10) weighed 203.4 g to 245.9 g (mean = 226.25 g) at the start of the test, while the Rep I females (10) weighed 217.9 g to 259.8 g (mean = 241.52 g). The Rep II test-group males (10) weighed 212.9 g to 289.6 g (mean = 229.68 g) at the start of the test, while the Rep II females (10) weighed 228.4 g to 275.6 g (mean = 237.97 g). The 5.74 g difference in mean weights between the sexes of the tested groups did not exceed the 50 g maximum that Protocol 1.217 permits for trials in which laboratory rats are used as subjects. The subjects were within the allowable weight range of 150 to 300 g. The control group was similarly comprised, with the males averaging 230.42 g (range 217.1-280.7 g) and the females 240.42 g (range 226.6-262.1 g) at the start of the study. The difference in average weights between all male and female rats in the test was12.32 g and did not exceed the 50 g maximum that Protocol 1.217 permits.

The bait-exposure phase of the bioassay began on 1/5/2004.

Results of the trial are summarized in Tables 1 through 3. All test-group animals died (100%) within 10 days of the onset of exposure to toxic bait. The 90% mortality criterion for a trial with fresh bait was met. A "...0% mortality rate occurred in the control group (after subtracting the single rat that escaped, consumed bait, and died).were reported for the control group." **The control group indeed had an escaped rat and lost one to toxic bait and is**

considered a 10% loss.

Mean body weights as reported by Mach were for the control rats, at the termination of the study, 294.6 g for the males and 260.3 g for the females. The mean body weights at death, of the male and female mice in each of the treatment groups were 241.6 g and 221.2 g (replicate I) and 232.9 g and 240.7 g (replicate II), respectfully.

Mach reports "The control group rats were offered challenge diet *ad libitum* for the entire exposure and post test periods. Consumption of the challenge diet was not measured. The test substance was offered for only 9 days because of all of the treatment rats had died, however, the control animals were still offered the challenge diet for the remainder of the exposure period. And the post-test period (day 20)." "The treatment group, replicate I rats consumed 39 place packs (or about 2,227 g) of Kaput Rat and Mouse Bait during the exposure period. The treatment group, replicate II rats consumed 35.5 place packs (or about 2,028 g) of Kaput Rat and Mouse Bait during the exposure period." page 13 of 90."

The test results are summarized below:

Table 1. Kaput Rat and Mouse Bait Place pack Penetration Studies with Norway Rats (RepI)

Pretest Weights		**15-Day Test-Consumption and Mortality**		
Sex	**Average Group Weight (g)**	**OPP Diet Consumed (g)**	**Treated Bait Consumed (g)**	**Total Bait Consumption (g)**
M (10)	226.25	NA	2341.51	NA
F (10)	241.52	**100% Mortality**		Percent **Toxic Bait** Consumed **NA**
Total (20)	Group Difference 15.27			

Table 2. Kaput Rat and Mouse Bait Placepack Penetration Studies with Norway Rats (RepII)

Pretest Weights		**15-Day Test-Consumption and Mortality**		
Sex	**Average Group Weight (g)**	**OPP Diet Consumed (g)**	**Treated Bait Consumed (g)**	**Total Bait Consumption (g)**
M (10)	229.68	NA	2055.96	NA
F (10)	237.97	**100% Mortality**		Percent **Toxic Bait** Consumed **NA**
Total (20)	Group Difference 8.29			

Efficacy Comments

1. In the guidelines, Standard Rat Anticoagulant Placepack Penetration Laboratory Method 1.217 (9-3-92), 1.1, and Standard House Mouse Anticoagulant Placepack Penetration Laboratory Method 1.218 (7-28-91), 1.1, the second sentence states: "Tests run according to this method must be supplemented by a test run according to OPP 1.203 Standard Norway Rat Anticoagulant Dry Bait Laboratory Test Method..." and "This test must be run in addition to OPP 1.204, Standard House Mouse Anticoagulant Dry Bait Laboratory Test Method, in which the toxic material is removed from the package (placepack) and tested separately (and presented in food containers).", respectively. This requirement is fulfilled by MRID 45662901 (and 46017801) for rats and MRID 45662904 for mice.

2. Both of the above studies are related and bait from the mixed batches of bait were used for both tests. The mixing batch records attached to the final report concur with the product it is meant to support (Kaput Rat and Mouse Bait). The mixing batch record is not referenced by the "Representative Chromatogram of a 25.1 ug/mL Warfarin Analytical Standard" attached to the final reports (pages 41 to 43). In future studies, please provide the raw data from the analytical notebook to link the analysis to the formulated bait and their chromatographic records.

3. Both of the studies discussed above obtained 100% mortality (MRIDs 463089-01 and -02). The studies are acceptable.

Conclusion(s): The laboratory efficacy studies for placepacks submitted in association with Kaput Rat and Mouse Bait (MRID numbers 463089-01 [03031] and 463089-02 [03030]) are acceptable. No label comments at this time.